Bactrim™ excels
(trimethoprim and sulfamethoxazole/Roche)

More urinary tract isolates prove sensitive *in vitro*

	Escherichia coli	Klebsiella pneumoniae	Proteus mirabilis	Proteus vulgaris	Proteus sp.	Enterobacter sp.	Enterobacter aerogenes	Enterobacter cloacae
BACTRIM TMP/SMX	96% 328,598†	89% 63,551	93% 62,691	84% 4174	91% 4381	88% 1736	96% 7326	92% 11,856
	72% 345,209	5% 65,466	85% 67,338	16% 4381	70% 4402	10% 1775	9% 7759	11% 12,091
CEPHALEXIN*	81% 343,339	85% 67,031	92% 67,027	16% 4398	80% 4365	22% 1834	13% 7571	12% 11,846
NITROFURANTOIN	97% 307,785	65% 61,162	7% 59,775	13% 3848	14% 3059	67% 1707	60% 7109	67% 10,830
	76% 322,304	78% 62,627	7% 62,340	31% 4177	4% 4266	69% 1635	86% 7262	79% 11,507

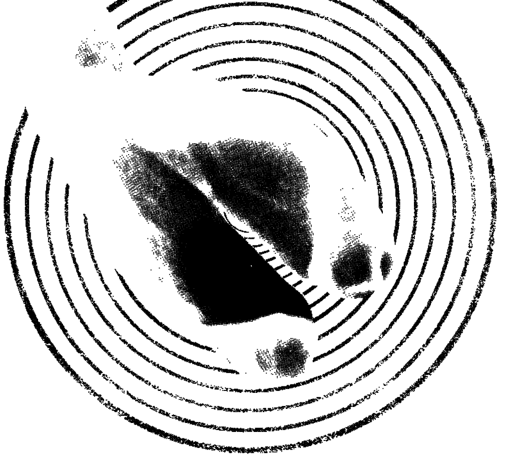
*Analogous to cephalothin, the primary antibiotic disc used in testing
†Numbers under percentages refer to the [illegible]
Source: The Bacteriology Report [illegible]

More studies show a lower incidence of bacteriologic recurrence

Patients treated with Bactrim have often remained free of recurrence longer than comparable patients treated with other drugs. In one study, 87 "difficult" patients, 76% of whom were infected with *E. coli*, were treated with Bactrim or cephalexin. Although the differences were not statistically significant, the cure rates with Bactrim were 85.4% at two weeks and 72.5% at six weeks, compared to 69.8% and [illegible] respectively, with cephalexin.

In a study of 96 women treated with either Bactrim or cephalexin for [illegible] *Proteus mirabilis* infections, the cure rate six weeks after the course of treatment remained significantly higher with Bactrim than with cephalexin (84.6% vs. 58.6% [illegible]).

Bactrim is indicated for the treatment of recurrent urinary tract infections due to susceptible strains of *Escherichia coli, Klebsiella, Enterobacter* and the *Proteus* species. However, it is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single antibacterial agent rather than the combination.



n recurrent urinary ract infections

More positive clinical results

Comparative studies of BACTRIM and other agents used in urinary tract infections

Reference	Number of Patients	Therapy	Dosage	Type of Study	Results
Cooper, Brumfitt, Hamilton-Miller (1980)[1]	41	Bactrim	160 mg trimethoprim & 800 mg sulfamethoxazole *b.i.d.*	Randomized comparison	Cure rate with Bactrim = 85.4%; with cephradine = 69.8% after two weeks
	43	cephradine	500 mg *q.i.d.*		
Gower, Tasker (1976)[2]	46	Bactrim	160 mg trimethoprim & 800 mg sulfamethoxazole *b.i.d.*	DB	Cure rate with Bactrim = 96%; with cephalexin = 68% two weeks after therapy
	47	cephalexin	1000 mg *b.i.d.*		
Cosgrove, Morrow (1974)[3]	15	Bactrim	160 mg trimethoprim & 800 mg sulfamethoxazole *b.i.d.*	DB	Bactrim proved more effective in uncomplicated chronic UTI
	15	ampicillin	500 mg *q.i.d.*		
Iravani *et al*[4] (1981)	64	Bactrim	160 mg trimethoprim & 800 mg sulfamethoxazole *b.i.d.*	Randomized comparison	Cure rate with Bactrim = 93%; with nalidixic acid = 90% one week after therapy
	71	nalidixic acid	1 Gm *q.i.d.*		
Schaeffer, Flynn, Jones[5] (1981)	20	Bactrim	160 mg trimethoprim & 800 mg sulfamethoxazole *b.i.d.*	Randomized comparison	Both agents equally effective
	20	cinoxacin	500 mg *b.i.d.*		

References: 1. Cooper J, Brumfitt W, Hamilton-Miller JMT: J Antimicrob Chemother 6:231-239, 1980. **2.** Gower PE, Tasker PRW: Br Med J 1:684-686, Mar 20, 1976. **3.** Cosgrove MD, Morrow JW: J Urol 111:670-672, May 1974. **4.** Iravani A et al: Antimicrob Agents Chemother 19:598-604, Apr 1981. **5.** Schaeffer AJ, Flynn S, Jones J: [illegible] 1981. **6.** Kramer MJ, Mauriz YF, Robertson TL, [illegible] MT: Microbiological studies [illegible] inhibitory and inhibitory doses of a sulfamethoxazole-trimethoprim combination [illegible] presented at the 12th International Congress of Chemotherapy, Florence, Italy, July 19-24, 1981.

Bactrim™ DS

(trimethoprim and sulfamethoxazole/Roche)

Economical *b.i.d.* therapy

ROCHE®

Please see summary of product information on the following page.

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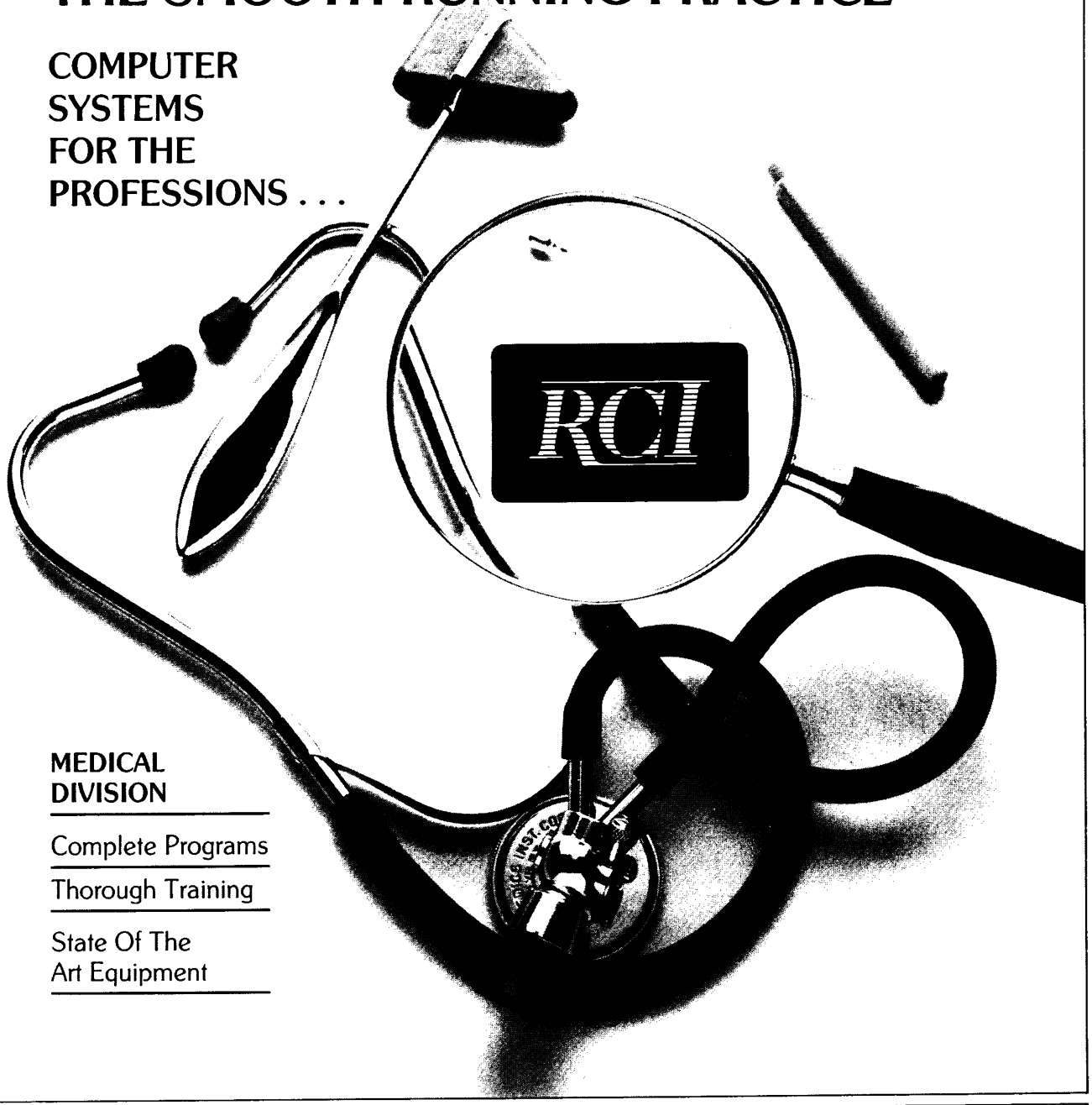

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superior staying power

serum levels with superior staying power

DURICEF® (cefadroxil) has up to twice the staying power of cephalexin, cefaclor and cephradine in serum, producing single-dose levels that last for 12 hours.[1]

urine levels with superior staying power

DURICEF has more than twice the staying power of cephalexin, cefaclor, and cephradine in urine, producing single-dose therapeutic levels that last up to 22 hours.[1]

a regimen with superior staying power

DURICEF with its once- or twice-a-day regimen has up to three times the staying power of antibiotics with t.i.d. or q.i.d. regimens, making possible compliance rates ranging from 70% to 93%.[2]

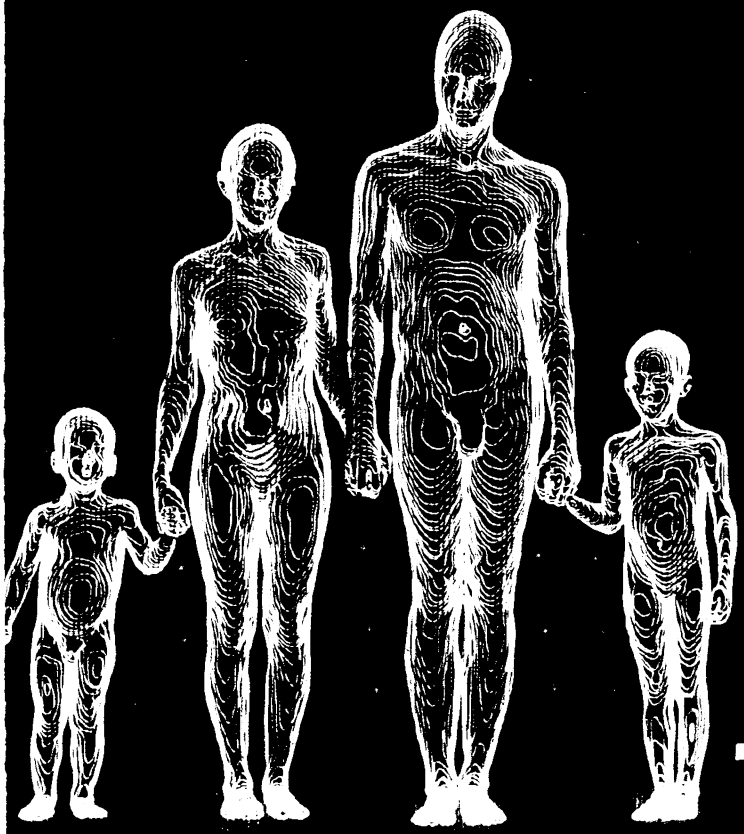
This advantage, along with excellent efficacy, will be appreciated by you and your patients when prescribing for infections* of the upper respiratory tract,† urinary tract, or skin and skin structure.

*Due to susceptible strains of indicated organisms.

†Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever.

1. Based on Manufacturers' Official Package Circulars.
2. Ayd, FJ Jr: Editorials. JAMA 1974; 230:263-264.

Mead Johnson PHARMACEUTICAL DIVISION



Extended action of DURICEF as represented by computer-generated simulation of serum concentration.

THE DIFFERENCE:

CAPSULES 500 mg
TABLETS 1 g

oral cephalosporin efficacy with once- or twice-a-day dosage that patients will stay with

Please see following page for brief summary of prescribing information.

 MJL 2-4780

CORGARD®
(nadolol tablets)
ONCE A DAY FOR HYPERTENSION

CORGARD® TABLETS
Nadolol Tablets

DESCRIPTION: Corgard (nadolol) is a synthetic nonselective beta-adrenergic receptor blocking agent.
CONTRAINDICATIONS: Bronchial asthma, sinus bradycardia and greater than first degree conduction block, cardiogenic shock, and overt cardiac failure (see WARNINGS).
WARNINGS: Cardiac Failure — Sympathetic stimulation may be a vital component supporting circulatory function in congestive heart failure, and its inhibition by beta-blockade may precipitate more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary, they can be used with caution in patients with a history of failure who are well-compensated, usually with digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle. IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta-blockers can, in some cases, lead to cardiac failure; therefore, at first sign or symptom of heart failure, digitalize and/or give diuretics, and closely observe response, or discontinue nadolol (gradually if possible).

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal — Hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after *abrupt* discontinuation of such therapy. When discontinuing chronic use of nadolol, particularly in patients with ischemic heart disease, gradually reduce dosage over a 1- to 2-week period and carefully monitor the patient. Reinstitute nadolol promptly (at least temporarily) and take other measures appropriate for management of unstable angina if angina markedly worsens or acute coronary insufficiency develops. Warn patients not to interrupt or discontinue therapy without physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue nadolol therapy abruptly even in patients treated only for hypertension.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA-BLOCKERS. Administer nadolol with caution since it may block bronchodilation produced by endogenous or exogenous catecholamine stimulation of $beta_2$ receptors.
Major Surgery — Because beta blockade impairs the ability of the heart to respond to reflex stimuli and may increase risks of general anesthesia and surgical procedures, resulting in protracted hypotension or low cardiac output, it has generally been suggested that such therapy should be withdrawn several days prior to surgery. Recognition of the increased sensitivity to catecholamines of patients recently withdrawn from beta-blocker therapy, however, has made this recommendation controversial. If possible, withdraw beta-blockers well before surgery takes place. In emergency surgery, inform the anesthesiologist that the patient is on beta-blocker therapy. Use of beta-receptor agonists such as isoproterenol, dopamine, dobutamine, or levarterenol can reverse the effects of nadolol. Difficulty in restarting and maintaining the heart beat has also been reported with beta-adrenergic receptor blocking agents.
Diabetes and Hypoglycemia — Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (e.g., tachycardia and blood pressure changes) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces release of insulin in response to hyperglycemia; therefore, it may be necessary to adjust dose of antidiabetic drugs.
Thyrotoxicosis — Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. To avoid abrupt withdrawal of beta-adrenergic blockade which might precipitate a thyroid storm, carefully manage patients suspected of developing thyrotoxicosis.
PRECAUTIONS: Impaired Hepatic or Renal Function — Use nadolol with caution in presence of either of these conditions (see DOSAGE AND ADMINISTRATION section of package insert).
Information for Patients — Warn patients, especially those with evidence of coronary artery insufficiency, against interruption or discontinuation of nadolol without physician's advice. Although cardiac failure rarely occurs in properly selected patients, advise patients being treated with beta-adrenergic blocking agents to consult physician at first sign or symptom of impending failure.
Drug Interactions — Catecholamine-depleting drugs (e.g., reserpine) may have an additive effect when given with beta-blocking agents. When treating patients with nadolol plus a catecholamine-depleting agent, carefully observe for evidence of hypotension and/or excessive bradycardia which may produce vertigo, syncope, or postural hypotension.
Carcinogenesis, Mutagenesis, Impairment of Fertility — In 1 to 2 years' oral toxicologic studies in mice, rats, and dogs, nadolol did not produce significant toxic effects. In 2-year oral carcinogenic studies in rats and mice, nadolol did not produce neoplastic, preneoplastic, or nonneoplastic pathologic lesions.
Pregnancy — In animal reproduction studies with nadolol, evidence of embryo- and fetotoxicity was found in rabbits (but not in rats or hamsters) at doses 5 to 10 times greater (on a mg/kg basis) than maximum indicated human dose; no teratogenic potential was seen in any of these species. There are no well-controlled studies in pregnant women; therefore, use nadolol in pregnant women only if potential benefit justifies potential risk to the fetus.
Nursing Mothers — It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when nadolol is administered to a nursing woman. Animal studies showed that nadolol is found in the milk of lactating rats.
Pediatric Use — Safety and effectiveness in children have not been established.
ADVERSE REACTIONS: Most adverse effects have been mild and transient and have rarely required nadolol withdrawal.
Cardiovascular — Bradycardia with heart rates of less than 60 beats per minute occurs commonly, and heart rates below 40 beats per minute and/or symptomatic bradycardia were seen in about 2 of 100 patients. Symptoms of peripheral vascular insufficiency, usually of the Raynaud type, have occurred in approximately 2 of 100 patients. Cardiac failure, hypotension, and rhythm/conduction disturbances have each occurred in about 1 of 100 patients. Single instances of first degree and third degree heart block have been reported; intensification of AV block is a known effect of beta-blockers (see also CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS). **Central Nervous System —** Dizziness or fatigue reported in approximately 2 of 100 patients; paresthesias, sedation, and change in behavior reported in approximately 6 of 1000 patients. **Respiratory —** Bronchospasm reported in approximately 1 of 1000 patients (see CONTRAINDICATIONS and WARNINGS). **Gastrointestinal —** Nausea, diarrhea, abdominal discomfort, constipation, vomiting, indigestion, anorexia, bloating, and flatulence each reported in 1 to 5 of 1000 patients. **Miscellaneous —** Each of the following reported in 1 to 5 of 1000 patients: rash; pruritus; headache; dry mouth, eyes, or skin; impotence or decreased libido; facial swelling; weight gain; slurred speech; cough; nasal stuffiness; sweating; tinnitus; blurred vision. Although relationship to drug usage is not clear, sleep disturbances have been reported. The oculomucocutaneous syndrome associated with practolol has not been reported with nadolol.
Potential Adverse Effects: Although other adverse effects reported with other beta-adrenergic blocking agents have not been reported with nadolol, they should be considered potential adverse effects of nadolol. **Central Nervous System —** reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place; short-term memory loss, emotional lability with slightly clouded sensorium; decreased performance on neuropsychometrics. **Gastrointestinal —** mesenteric arterial thrombosis; ischemic colitis. **Hematologic —** agranulocytosis; thrombocytopenic or nonthrombocytopenic purpura. **Allergic —** fever combined with aching and sore throat; laryngospasm; respiratory distress. **Miscellaneous —** reversible alopecia; Peyronie's disease; erythematous rash.
OVERDOSAGE: Nadolol can be removed from the general circulation by hemodialysis. In addition to gastric lavage, employ the following measures as appropriate. In determining duration of corrective therapy, take note of long duration of effect of nadolol.
Excessive Bradycardia — Administer atropine (0.25 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
Cardiac Failure — Administer a digitalis glycoside and diuretic. It has been reported that glucagon may also be useful in this situation.
Hypotension — Administer vasopressors, e.g., epinephrine or levarterenol. (There is evidence that epinephrine may be the drug of choice.)
Bronchospasm — Administer a $beta_2$-stimulating agent and/or a theophylline derivative.
DOSAGE: For all patients, DOSAGE MUST BE INDIVIDUALIZED.
For **angina pectoris,** usual initial dose is 40 mg q.d.; gradually increase in 40 to 80 mg increments at 3 to 7 day intervals until optimum clinical response or pronounced slowing of the heart rate; usual maintenance dose is 80 to 240 mg q.d. (most patients respond to 160 mg or less daily). If treatment is to be discontinued, reduce dosage gradually over a period of 1 to 2 weeks (see WARNINGS).
For **hypertension,** usual initial dose is 40 mg q.d.; gradually increase in 40 to 80 mg increments until optimum blood pressure reduction is achieved; usual maintenance dose is 80 to 320 mg q.d. (rarely, doses up to 640 mg may be needed).
Patients with renal failure require adjustment in dosing interval; see package insert for dosage in these patients.
For full prescribing information, consult package insert.
HOW SUPPLIED: In scored tablets containing 40, 80, 120, or 160 mg nadolol per tablet in bottles of 100 and 1000 tablets and in Unimatic® unit-dose packs of 100 tablets. The 40 mg and 80 mg tablets are also available in convenience packages containing 4 blister cards of 7 tablets each.

SQUIBB®

513-513

Issued: July 1983

Less chance of depression, insomnia and nightmares than propranolol

Because hydrophilic (water-soluble) Corgard™ (nadolol tablets) does not readily cross the blood-brain barrier, CNS side effects should occur less frequently than with highly lipophilic propranolol.*

The most commonly reported CNS side effects of Corgard, dizziness and fatigue, have each been reported in approximately 2 of 100 patients receiving Corgard.*

Once-a-day Corgard is as effective as propranolol, qid, in both hypertension and angina pectoris.[1]

Once-a-day

CORGARD®
(nadolol tablets)

For a full discussion of CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS, and WARNINGS, including avoidance of abrupt withdrawal, please see brief summary.

. Data on file: Squibb Institute for Medical Research.

SQUIBB®

EQUALLY EFFECTIVE AND MORE PRACTICAL FOR HYPERTENSION

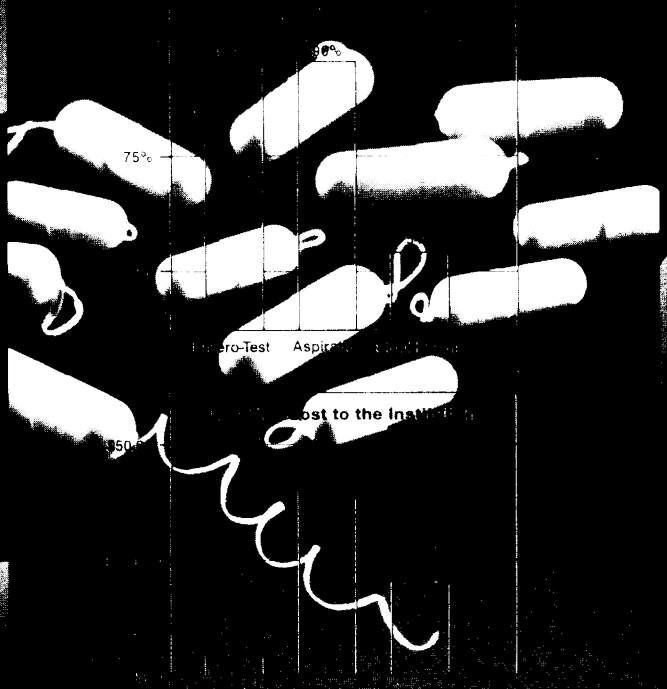
Please see adjacent page of this advertisement for brief summary.

THE ALTERNATIVE TO STOOL EXAMS.

ENTERO-TEST.®

ADULT AND PEDIATRIC

A 96% success rate in Giardia diagnosis.
80% plus accuracy for other duodenal parasites.



Entero-Test is a highly absorbant nylon line wound inside of a weighted gelatin capsule. The proximal end of the line is taped to the patient's cheek while the capsule works its way into the duodenum. Bile stained line is recovered and observed for parasites.

ENTERO-TEST® has the following advantages:

- Rapid
- Accurate
- Safe
- No Radiation
- Outpatient and Inpatient Use

Please send me more information about the Entero-Test. WJ7/85

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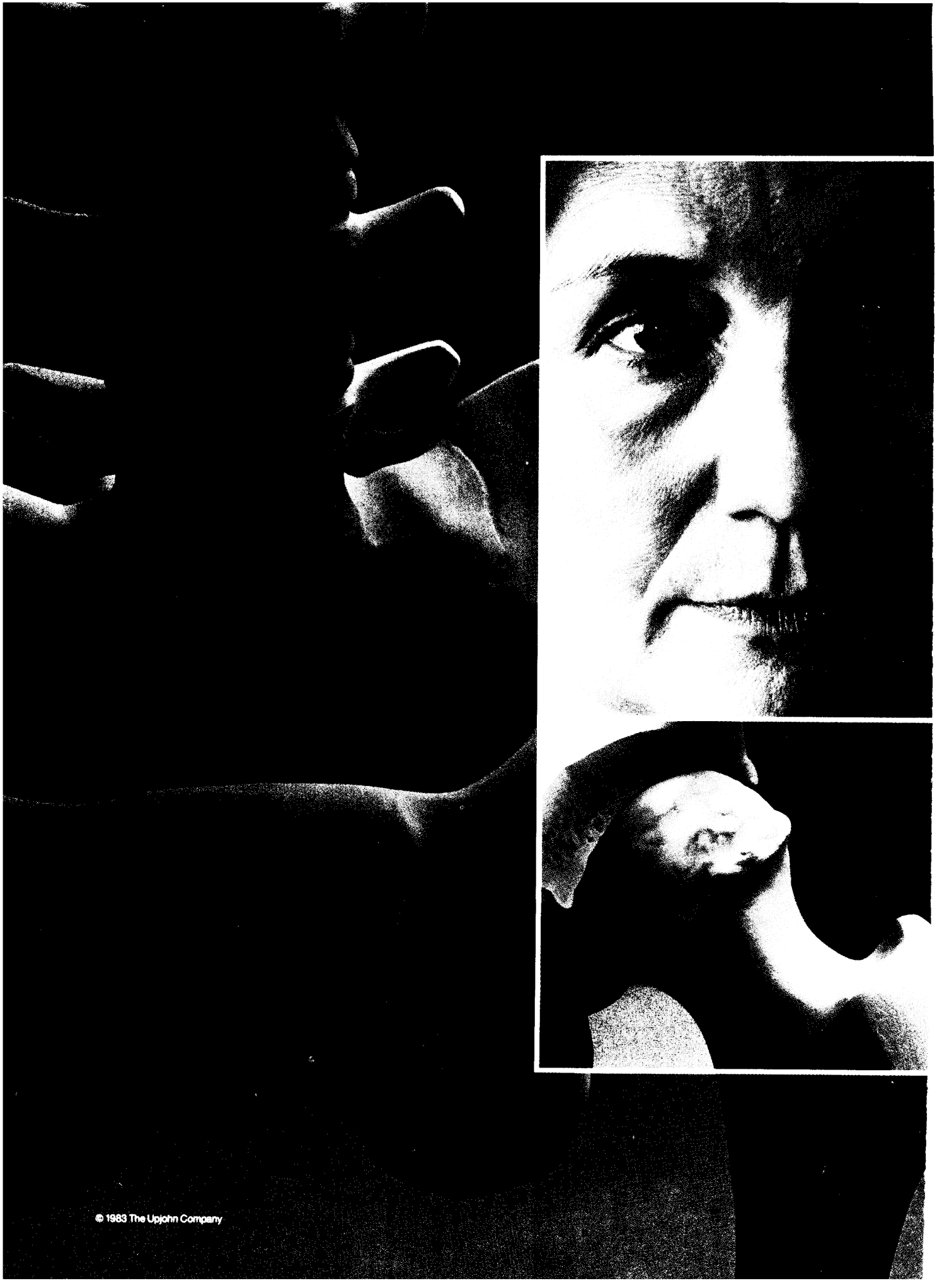


Arthritis pain after 50

Age is no barrier to the benefits of Motrin 600 mg tablets

The pain-relieving power of *Motrin* 600 mg tablets is welcome at any age. The advantages of *Motrin* become more important as patients grow older.

Advanced age has little or no influence on the pharmacokinetics of *Motrin.*

Motrin is as effective as indomethacin in relieving arthritis pain and inflammation. *Motrin* causes significantly fewer CNS effects and about half as many GI complaints as indomethacin.

Motrin relieves pain as effectively as a combination of aspirin 650 mg plus codeine 60 mg, as documented in analgesia studies.

Motrin has no significant effect on clotting factors in patients on coumarin-type anticoagulants in controlled studies. *Motrin* should be used with caution in persons with intrinsic coagulation defects and in those on anticoagulant therapy.

Motrin is rapidly metabolized and does not accumulate. *Motrin* provides better control of therapy, rapid response to dosage adjustment, and permits tailoring dosage to each patient's needs.

New: The Motrin Patient Brochure
An easy-to-read booklet, provided to physicians, that helps patients understand their arthritis therapy... encourages their cooperation.

Helping you to help your patients—
Ask your Upjohn Representative for a complimentary supply.

The confidence that comes from experience...good reason to prescribe

Motrin® 600 mg TABLETS
(ibuprofen)

One tablet t.i.d.

Please turn page for a brief summary of prescribing information.

Upjohn The Upjohn Company
Kalamazoo, Michigan 49001

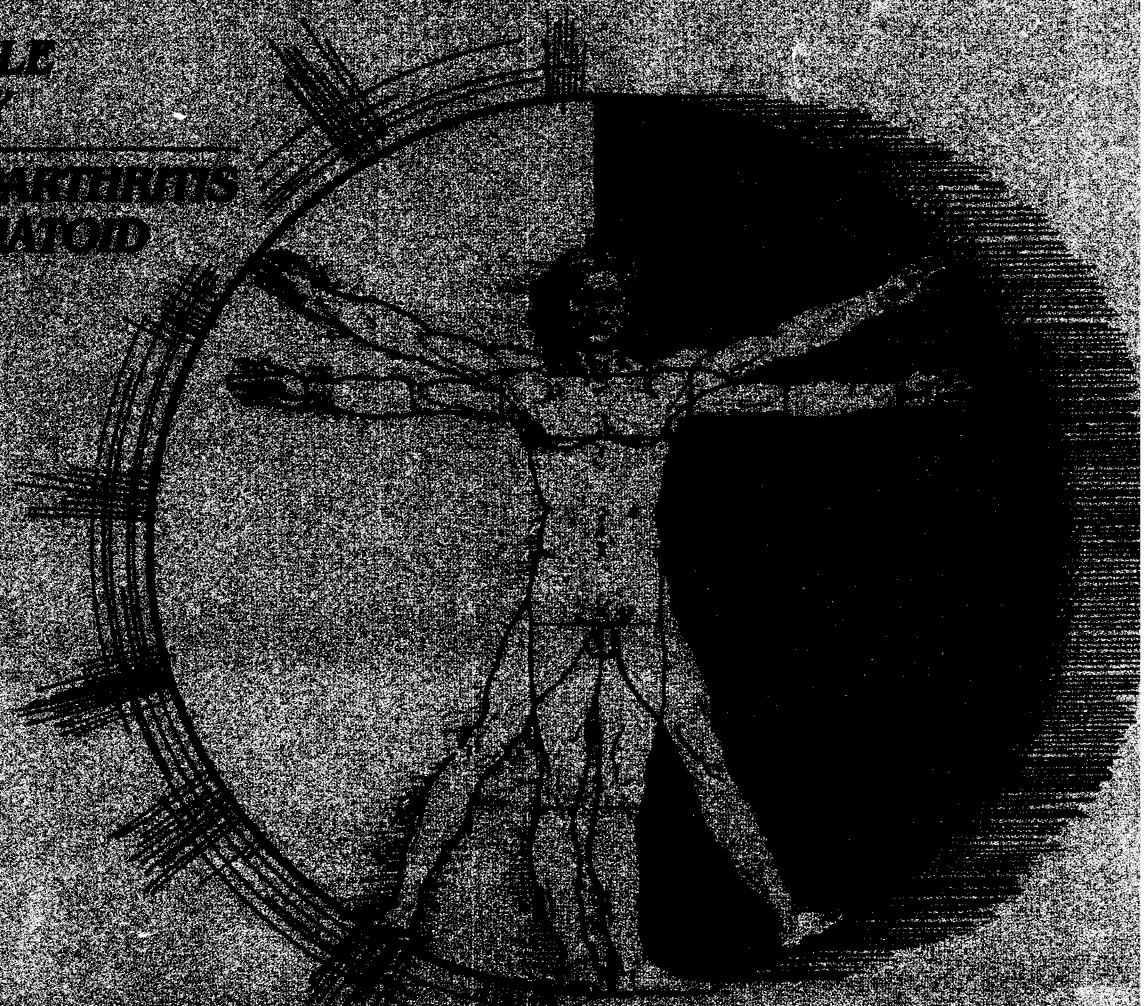
THE FIRST ONE-A-DAY ANTI-ARTHRITIC AGENT

Feldene®

(PIROXICAM) 20 mg capsules

ONE CAPSULE ONCE DAILY

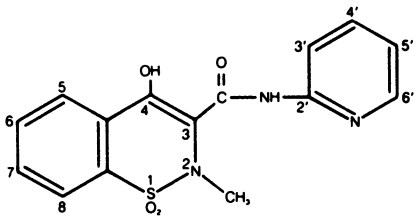
FOR OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS



Please see next page for FELDENE (piroxicam) prescribing information.

FELDENE® CAPSULES
(piroxicam)
For Oral Use

DESCRIPTION. FELDENE (piroxicam) is 4-Hydroxy-2-methyl-*N*-2-pyridinyl-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide, an oxicam. Members of the oxicam family are not carboxylic acids, but they are acidic by virtue of the enolic 4-hydroxy substituent. FELDENE occurs as a white crystalline solid, sparingly soluble in water, dilute acid and most organic solvents. It is slightly soluble in alcohols and in aqueous alkaline solution. It exhibits a weakly acidic 4-hydroxy proton (pKa 5.1) and a weakly basic pyridyl nitrogen (pKa 1.8). It has the following structure:



Molecular Formula: $C_{15}H_{13}N_3O_4S$ Molecular Weight: 331.35

CLINICAL PHARMACOLOGY. FELDENE has shown anti-inflammatory, analgesic and antipyretic properties in animals. Edema, erythema, tissue proliferation, fever, and pain can all be inhibited in laboratory animals by the administration of FELDENE. It is effective regardless of the etiology of the inflammation. The mode of action of FELDENE is not fully established at this time. However, a common mechanism for the above effects may exist in the ability of FELDENE to inhibit the biosynthesis of prostaglandins, known mediators of inflammation.

It is established that FELDENE does not act by stimulating the pituitary-adrenal axis.

FELDENE is well absorbed following oral administration. Drug plasma concentrations are proportional for 10 and 20 mg doses, generally peak within three to five hours after medication, and subsequently decline with a mean half-life of 50 hours (range of 30 to 86 hours, although values outside of this range have been encountered).

This prolonged half-life results in the maintenance of relatively stable plasma concentrations throughout the day on once daily doses and to significant drug accumulation upon multiple dosing. A single 20 mg dose generally produces peak piroxicam plasma levels of 1.5 to 2 mcg/ml, while maximum drug plasma concentrations, after repeated daily ingestion of 20 mg FELDENE, usually stabilize at 3-8 mcg/ml. Most patients approximate steady state plasma levels within 7 to 12 days. Higher levels, which approximate steady state at two to three weeks, have been observed in patients in whom longer plasma half-lives of piroxicam occurred.

FELDENE and its biotransformation products are excreted in urine and feces, with about twice as much appearing in the urine as the feces. Metabolism occurs by hydroxylation at the 5 position of the pyridyl side chain and conjugation of this product; by cyclodehydration; and by a sequence of reactions involving hydrolysis of the amide linkage, decarboxylation, ring contraction, and N-demethylation. Less than 5% of the daily dose is excreted unchanged.

Concurrent administration of aspirin (3900 mg/day) and FELDENE (20 mg/day), resulted in a reduction of plasma levels of piroxicam to about 80% of their normal values. The use of FELDENE in conjunction with aspirin is not recommended because data are inadequate to demonstrate that the combination produces greater improvement than that achieved with aspirin alone and the potential for adverse reactions is increased. Concomitant administration of antacids had no effect on FELDENE plasma levels. The effects of impaired renal function or hepatic disease on plasma levels have not been established.

FELDENE, like salicylates and other nonsteroidal anti-inflammatory agents, is associated with symptoms of gastrointestinal tract irritation (see ADVERSE REACTIONS). However, in a study utilizing ^{51}Cr-tagged red blood cells, 20 mg of FELDENE administered as a single dose for four days did not result in a significant increase in fecal blood loss and did not detectably affect the gastric mucosa. In the same study a total daily dose of 3900 mg of aspirin, i.e., 972 mg q.i.d., caused a significant increase in fecal blood loss and mucosal lesions as demonstrated by gastroscopy.

In controlled clinical trials, the effectiveness of FELDENE has been established for both acute exacerbations and long-term management of rheumatoid arthritis and osteoarthritis.

The therapeutic effects of FELDENE are evident early in the treatment of both diseases with a progressive increase in response over several (8-12) weeks. Efficacy is seen in terms of pain relief and, when present, subsidence of inflammation.

Doses of 20 mg/day FELDENE display a therapeutic effect comparable to therapeutic doses of aspirin, with a lower incidence of minor gastrointestinal effects and tinnitus.

FELDENE has been administered concomitantly with fixed doses of gold and corticosteroids. The existence of a "steroid-sparing" effect has not been adequately studied to date.

INDICATIONS AND USAGE. FELDENE is indicated for acute or long-term use in the relief of signs and symptoms of the following:

1. osteoarthritis
2. rheumatoid arthritis

Dosage recommendations for use in children have not been established.

CONTRAINDICATIONS. FELDENE should not be used in patients who have previously exhibited hypersensitivity to it, or in individuals with the syndrome comprised of bronchospasm, nasal polyps, and angioedema precipitated by aspirin or other nonsteroidal anti-inflammatory drugs.

WARNINGS. Peptic ulceration, perforation, and G.I. bleeding—sometimes severe, and, in rare instances fatal—have been reported with patients receiving FELDENE. If FELDENE must be given to patients with a history of upper gastrointestinal tract disease, the patient should be under close supervision (see ADVERSE REACTIONS). In controlled clinical trials, incidence of peptic ulceration with the maximum recommended FELDENE capsule dose of 20 mg per day was 0.8%. The use of doses higher than the recommended dose is associated with an increase in the incidence of gastrointestinal irritation and ulcers.

PRECAUTIONS. As with other anti-inflammatory agents, long-term administration to animals results in renal papillary necrosis and related pathology in rats, mice, and dogs.

As with other drugs that inhibit prostaglandin biosynthetase, reversible elevations of BUN have been reported in clinical studies with FELDENE. The effect is thought to result from inhibition of renal prostaglandin synthesis resulting in a change in medullary and deep cortical blood flow with an attendant effect on renal function. Because of the extensive renal excretion of piroxicam, patients with impaired renal function should be carefully monitored.

Although other nonsteroidal anti-inflammatory drugs do not have the same direct effects on platelets that aspirin does, all drugs inhibiting prostaglandin biosynthesis do interfere with platelet function to some degree; therefore, patients who may be adversely affected by such an action should be carefully observed when FELDENE is administered.

Because of reports of adverse eye findings with nonsteroidal anti-inflammatory agents, it is recommended that patients who develop visual complaints during treatment with FELDENE have ophthalmic evaluation.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. The SGPT (ALT) test is probably the most sensitive indicator of liver dysfunction. Meaningful (3 times the upper limit of normal) elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with FELDENE. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with other nonsteroidal anti-inflammatory drugs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), FELDENE should be discontinued. (See also ADVERSE REACTIONS.)

Less than 1.0% of patients receiving FELDENE (piroxicam) have shown reversible elevation of one or more liver function parameters. While concurrent aspirin may have been involved in some of these changes, a relationship to FELDENE could not be excluded. Studies in patients with impaired liver function have not been done.

Although at the recommended dose of 20 mg/day of FELDENE increased fecal blood loss due to gastrointestinal irritation did not occur (see CLINICAL PHARMACOLOGY), in about 4% of the patients treated with FELDENE alone or concomitantly with aspirin, reductions in hemoglobin and hematocrit values were observed. Therefore, these values should be determined if signs or symptoms of anemia occur.

Peripheral edema has been observed in approximately 2% of the patients treated with FELDENE. Therefore, as with other nonsteroidal anti-inflammatory drugs, FELDENE should be used with caution in patients with compromised cardiac function, hypertension or other conditions predisposing to fluid retention.

DRUG INTERACTIONS. FELDENE is highly protein bound, and, therefore, might be expected to displace other protein-bound drugs. Although *in vitro* studies have shown this not to occur with dicoumarol, physicians should closely monitor patients for a change in dosage requirements when administering FELDENE to patients on coumarin-type anticoagulants and other highly protein-bound drugs.

Plasma levels of piroxicam are depressed to approximately 80% of their normal values when FELDENE is administered in conjunction with aspirin (3900 mg/day), but concomitant administration of antacids has no effect on piroxicam plasma levels (see CLINICAL PHARMACOLOGY).

Carcinogenesis, Chronic Animal Toxicity and Impairment of Fertility: Subacute and chronic toxicity studies have been carried out in rats, mice, dogs, and monkeys.

The pathology most often seen was that characteristically associated with the animal toxicology of anti-inflammatory agents: renal papillary necrosis (see PRECAUTIONS) and gastrointestinal lesions.

In classical studies in laboratory animals piroxicam did not show any teratogenic potential. Reproductive studies revealed no impairment of fertility in animals.

Pregnancy and Nursing Mothers: Like other drugs which inhibit the synthesis and release of prostaglandins, piroxicam increased the incidence of dystocia and delayed parturition in pregnant animals when piroxicam administration was continued late into pregnancy. Gastrointestinal tract toxicity was increased in pregnant females in the last trimester of pregnancy compared to non-pregnant females or females in earlier trimesters of pregnancy.

FELDENE is not recommended for use in nursing mothers or in pregnant women because of the animal findings and since safety for such use has not been established in humans.

Use in Children: Dosage recommendations and indications for use in children have not been established.

ADVERSE REACTIONS. The incidence of adverse reactions to piroxicam is based on clinical trials involving approximately 2300 patients, about 400 of whom were treated for more than one year and 170 for more than two years. About 30% of all patients receiving daily doses of 20 mg of FELDENE experienced side effects. Gastrointestinal symptoms were the most prominent side effects—occurring in approximately 20% of the patients, which in most instances did not interfere with the course of therapy. Of the patients experiencing gastrointestinal side effects, approximately 5% discontinued therapy with an overall incidence of peptic ulceration of about 1%.

Other than the gastrointestinal symptoms, edema, dizziness, headache, changes in hematological parameters, and rash have been reported in a small percentage of patients. Routine ophthalmoscopy and slit-lamp examinations have revealed no evidence of ocular changes in 205 patients followed from 3 to 24 months while on therapy.

Adverse reactions are listed below by body system for all patients in clinical trials with FELDENE at doses of 20 mg/day.

Incidence Greater Than 1% The following adverse reactions occurred more frequently than 1 in 100.

Gastrointestinal: stomatitis, anorexia, epigastric distress*, nausea*, constipation, abdominal discomfort, flatulence, diarrhea, abdominal pain, and indigestion.

Hematological: decreases in hemoglobin* and hematocrit* (see PRECAUTIONS), leucopenia, eosinophilia.

Urogenital: BUN elevations (see PRECAUTIONS)

Central Nervous System: dizziness, somnolence, vertigo

Special Senses: tinnitus

Body as a Whole: headache, malaise

Cardiovascular/Respiratory: edema (see PRECAUTIONS)

Dermatologic: pruritus, rash

*Reactions occurring in 3% to 6% of patients treated with FELDENE.

Incidence Less Than 1% (Causal Relationship Probable)

The following adverse reactions occurred less frequently than 1 in 100. The probability exists that there is a causal relationship between FELDENE and these reactions.

Gastrointestinal: liver function abnormalities (see PRECAUTIONS), vomiting, hematemesis, melena, gastrointestinal bleeding, perforation and ulceration, and dry mouth

Hematological: thrombocytopenia

Dermatologic: sweating, erythema, bruising, desquamation, erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome, photoallergic skin reactions

Special Senses: swollen eyes, blurred vision, eye irritations

Body as a Whole: pain (colic)

Cardiovascular/Respiratory: hypertension (see PRECAUTIONS)

Urogenital: hematuria

Metabolic: hypoglycemia, weight increase, weight decrease

Central Nervous System: depression, insomnia, nervousness

Incidence Less Than 1% (Causal Relationship Unknown)

Other adverse reactions were reported with a frequency of less than 1 in 100, but a causal relationship between FELDENE and the reaction could not be determined.

Cardiovascular/Respiratory: palpitations, dyspnea

Central Nervous System: akathisia

Urogenital System: dysuria

Hematological: aplastic anaemia

OVERDOSAGE. In the event treatment for overdosage is required the long plasma half-life (see CLINICAL PHARMACOLOGY) of piroxicam should be considered. The absence of experience with acute overdosage precludes characterization of sequelae and recommendation of specific antidotal efficacy at this time. It is reasonable to assume, however, that the standard measures of gastric evacuation and general supportive therapy would apply.

ADMINISTRATION AND DOSAGE. Rheumatoid Arthritis, Osteoarthritis:

It is recommended that FELDENE therapy be initiated and maintained at a single daily dose of 20 mg. If desired, the daily dose may be divided. Because of the long half-life of FELDENE, steady-state blood levels are not reached for 7-12 days. Therefore, although the therapeutic effects of FELDENE are evident early in treatment, there is a progressive increase in response over several weeks and the effect of therapy should not be assessed for two weeks.

Dosage recommendations and indications for use in children have not been established.

HOW SUPPLIED. FELDENE Capsules for oral administration.

Bottles of 100: 10 mg (NDC 0069-3220-66) maroon and blue #322
20 mg (NDC 0069-3230-66) maroon #323

Bottles of 500: 20 mg (NDC 0069-3230-73) maroon #323

Unit dose packages of 100: 20 mg (NDC 0069-3230-41) maroon #323

Revised November 1982

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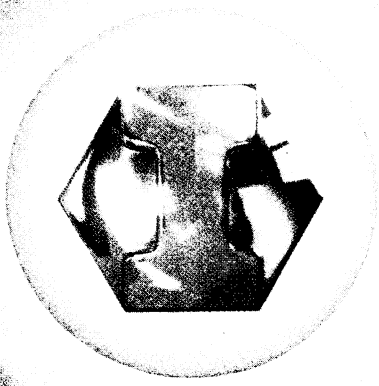

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INDERAL, a logical first step

Unlike thiazide diuretics, which can provoke serious reductions of serum potassium, INDERAL has been found to maintain or modestly increase serum potassium levels.[1,2] Therefore, the consequences of hypokalemia—including the threat of ventricular arrhythmias[2]—may be significantly reduced.

INDERAL acts to reduce catecholamine-induced "spiking" of blood pressure which often coincides with the physical and emotional stress in a hypertensive's life.[3] INDERAL reduces elevated heart rate, force of ventricular contraction, and cardiac work load—providing smooth control of hypertension to decrease the risk of related cardiovascular complications. (INDERAL should not be used in the presence of congestive heart failure, sinus bradycardia, heart block greater than first degree, or bronchial asthma.)

INDERAL works in a way that non-beta blockers can't—to provide long-term cardiovascular benefits.

INDERAL provides treatment for coexisting angina pectoris or cardiac arrhythmias in addition to reducing blood pressure—for comprehensive protection. What's more, INDERAL is well tolerated, acting with few of the distressing side effects of antihypertensive agents such as methyldopa or reserpine. Impotence, depression, sedation, orthostatic hypotension, and nasal stuffiness are rare. (Please see following page for Brief Summary of Prescribing Information, including side effects of INDERAL.)

Indeed, INDERAL has changed the face of antihypertensive therapy, worldwide. And it continues to do so—with an unparalleled record of clinical efficacy and experience.

INDERAL. It's the kind of protection hypertensive patients need—right from the start.

References: 1. Traub, Y. M., *et al.*: Clin. Pharmacol. Ther. *28*:765 (Dec.) 1980. 2. Hollifield, S.W., and Slaton, R.E.: Acta Med. Scand. *647* (Suppl.):67, 1981. 3. Cohen, J.D.: Propranolol vs. diuretics in initial therapy for hypertension. Medical Education Programs Ltd., Ayerst Laboratories, 1982.

INDERAL®
(PROPRANOLOL HCl)

Comprehensive Cardiovascular Protection

Please see following page for brief summary of prescribing information.

THE MOST WIDELY PRESCRIBED BETA BLOCKER IN THE WORLD

INDERAL®

(PROPRANOLOL HCl)

B.I.D. FOR HYPERTENSION

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BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)
The appearance of these tablets is a trademark of Ayerst Laboratories.
Inderal® (propranolol hydrochloride)

BEFORE USING INDERAL (PROPRANOLOL HYDROCHLORIDE), THE PHYSICIAN SHOULD BE THOROUGHLY FAMILIAR WITH THE BASIC CONCEPT OF ADRENERGIC RECEPTORS (ALPHA AND BETA), AND THE PHARMACOLOGY OF THIS DRUG.

CONTRAINDICATIONS

Propranolol hydrochloride is contraindicated in 1) bronchial asthma; 2) allergic rhinitis during the pollen season; 3) sinus bradycardia and greater than first degree block; 4) cardiogenic shock; 5) right ventricular failure secondary to pulmonary hypertension; 6) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with propranolol; 7) in patients on adrenergic-augmenting psychotropic drugs (including MAO inhibitors), and during the two week withdrawal period from such drugs.

WARNINGS

CARDIAC FAILURE: Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure, and inhibition with beta-blockade always carries the potential hazard of further depressing myocardial contractility and precipitating cardiac failure. Propranolol acts selectively without abolishing the inotropic action of digitalis on the heart muscle (i.e., that of supporting the strength of myocardial contractions). In patients already receiving digitalis, the positive inotropic action of digitalis may be reduced by propranolol's negative inotropic effect. The effects of propranolol and digitalis are additive in depressing AV conduction.

IN PATIENTS WITHOUT A HISTORY OF CARDIAC FAILURE, continued depression of the myocardium over a period of time, can, in some cases, lead to cardiac failure. In rare instances, this has been observed during propranolol therapy. Therefore, at the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or given a diuretic, and the response observed closely: a) if cardiac failure continues, despite adequate digitalization and diuretic therapy, propranolol therapy should be immediately withdrawn; b) if tachyarrhythmia is being controlled, patients should be maintained on combined therapy and the patient closely followed until threat of cardiac failure is over.

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following *abrupt* discontinuation of propranolol therapy. Therefore, when discontinuance of propranolol is planned the dosage should be gradually reduced and the patient carefully monitored. In addition, when propranolol is prescribed for angina pectoris, the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If propranolol therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute propranolol therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease, who are given propranolol for other indications.

IN PATIENTS WITH THYROTOXICOSIS, possible deleterious effects from long-term use have not been adequately appraised. Special consideration should be given to propranolol's potential for aggravating congestive heart failure. Propranolol may mask the clinical signs of developing or continuing hyperthyroidism or complications and give a false impression of improvement. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. This is another reason for withdrawing propranolol slowly. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

IN PATIENTS UNDERGOING MAJOR SURGERY, beta-blockade impairs the ability of the heart to respond to reflex stimuli. For this reason, with the exception of pheochromocytoma, propranolol should be withdrawn 48 hours prior to surgery at which time all chemical and physiologic effects are gone according to available evidence. However, in case of emergency surgery, since propranolol is a competitive inhibitor of beta-receptor agonists, its effects can be reversed by administration of such agents, e.g., isoproterenol or levarterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in restarting and maintaining the heart beat has also been reported.

IN PATIENTS PRONE TO NONALLERGIC BRONCHOSPASM (*e.g.*, CHRONIC BRONCHITIS. EMPHYSEMA), propranolol should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

DIABETICS AND PATIENTS SUBJECT TO HYPOGLYCEMIA: Because of its beta-adrenergic blocking activity, propranolol may prevent the appearance of premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia. This is especially important to keep in mind in patients with labile diabetes. Hypoglycemic attacks may be accompanied by a precipitous elevation of blood pressure.

USE IN PREGNANCY: The safe use of propranolol in human pregnancy has not been established. Use of any drug in pregnancy or women of childbearing potential requires that the possible risk to mother and/or fetus be weighed against the expected therapeutic benefit. Embryotoxic effects have been seen in animal studies at doses about 10 times the maximum recommended human dose.

PRECAUTIONS

Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if propranolol is administered. The added catecholamine-blocking action of this drug may then produce an excessive reduction of the resting sympathetic nervous activity. Occasionally, the pharmacologic activity of propranolol may produce hypotension and/or marked bradycardia resulting in vertigo, syncopal attacks, or orthostatic hypotension.

As with any new drug given over prolonged periods, laboratory parameters should be observed at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function.

ADVERSE REACTIONS

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; arterial insufficiency, usually of the Raynaud type; thrombocytopenic purpura. *Central Nervous System:* lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics. *Gastrointestinal:* nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis. *Allergic:* pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress. *Respiratory:* bronchospasm. *Hematologic:* agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura. *Miscellaneous:* reversible alopecia. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta-blocker (practolol) have not been conclusively associated with propranolol. *Clinical Laboratory Test Findings:* Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

HOW SUPPLIED

INDERAL (propranolol hydrochloride)

TABLETS

—Each hexagonal-shaped, orange, scored tablet is embossed with an "I" and imprinted with "INDERAL 10," contains **10 mg** propranolol hydrochloride, in bottles of 100 (NDC 0046-0421-81) and 1,000 (NDC 0046-0421-91). Also in unit dose package of 100 (NDC 0046-0421-99).

—Each hexagonal-shaped, blue, scored tablet is embossed with an "I" and imprinted with "INDERAL 20," contains **20 mg** propranolol hydrochloride, in bottles of 100 (NDC 0046-0422-81) and 1,000 (NDC 0046-0422-91). Also in unit dose package of 100 (NDC 0046-0422-99).

—Each hexagonal-shaped, green, scored tablet is embossed with an "I" and imprinted with "INDERAL 40," contains **40 mg** propranolol hydrochloride, in bottles of 100 (NDC 0046-0424-81) and 1,000 (NDC 0046-0424-91). Also in unit dose package of 100 (NDC 0046-0424-99).

—Each hexagonal-shaped, pink, scored tablet is embossed with an "I" and imprinted with "INDERAL 60," contains **60 mg** propranolol hydrochloride, in bottles of 100 (NDC 0046-0426-81) and 1,000 (NDC 0046-0426-91), and in unit dose packages of 100 (NDC 0046-0426-99).

—Each hexagonal-shaped, yellow, scored tablet is embossed with an "I" and imprinted with "INDERAL 80," contains **80 mg** propranolol hydrochloride, in bottles of 100 (NDC 0046-0428-81) and 1,000 (NDC 0046-0428-91). Also in unit dose package of 100 (NDC 0046-0428-99).

The appearance of these tablets is a trademark of Ayerst Laboratories.

Store at room temperature (approximately 25° C).

INJECTABLE

—Each ml contains 1 mg of propranolol hydrochloride in Water for Injection. The pH is adjusted with citric acid. Supplied as: 1 ml ampuls in boxes of 10 (NDC 0046-3265-10).

Store at room temperature (approximately 25° C).

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"I can do things that I couldn't do for 3 yrs. including joining the human race again."

"My daily routine consisted of sitting in my chair trying to stay alive."

"My doctor switched me to PROCARDIA[*] *as soon as it became available. The change in my condition is remarkable."*

"I shop, cook and can plant flowers again."

"I have been able to do volunteer work...and feel needed and useful once again."

PROCARDIA can mean the return to a more normal life for your patients—having fewer anginal attacks,[1] taking fewer nitroglycerin tablets,[2] doing more, and being more productive once again.

Side effects are usually mild (most frequently reported are dizziness or lightheadedness, peripheral edema, nausea, weakness, headache and flushing, each occurring in about 10% of patients; transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%).

for the varied faces of angina

* Procardia is indicated for the management of:
1) Confirmed vasospastic angina.
2) Angina where the clinical presentation suggests a possible vasospastic component.
3) Chronic stable angina without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and or nitrates or who cannot tolerate these agents. In chronic stable angina (effort-associated angina) PROCARDIA has been effective in controlled trials of up to eight weeks' duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in these patients are incomplete.

PROCARDIA®
(NIFEDIPINE) *Capsules 10 mg*

Please see PROCARDIA *brief summary on adjoining page.*

THE EXPERTS AGREE...

ZYLOPRIM® (allopurinol) IS SIMPLE, EFFECTIVE GOUT THERAPY

Unlike uricosuric agents, Zyloprim® (allopurinol) is clearly the choice for:

OVERPRODUCERS/ UNDEREXCRETERS

"One recent suggestion is that overproducers of uric acid are more 'appropriately' treated with allopurinol and underexcreters with uricosuric drugs. Such an argument is superficially attractive but may be specious: most patients with gout... may nevertheless be managed perfectly well with allopurinol."[1]

—G. Boss, MD et al

TOPHI, CALCULI, RENAL DISEASE

"... (1) patients with extensive tophaceous disease...; (2) patients with a history of renal calculi... since a uricosuric drug may exacerbate renal stone disease; and (3) patients with significant renal disease... who are unlikely to respond to a uricosuric drug."[2]

—Edward W. Holmes, Jr, MD

For information on adverse reactions, warnings, etc, please see brief summary of prescribing information below.

ZYLOPRIM® (allopurinol)
100 and 300 mg Scored Tablets

INDICATIONS AND USE: This is not an innocuous drug and strict attention should be given to the indications for its use. Pending further investigation, its use in other hyperuricemic states is not indicated at this time.
Zyloprim® (allopurinol) is intended for:
1. treatment of gout, either primary, or secondary to the hyperuricemia associated with blood dyscrasias and their therapy;
2. treatment of primary or secondary uric acid nephropathy, with or without accompanying symptoms of gout;
3. treatment of patients with recurrent uric acid stone formation;
4. prophylactic treatment to prevent tissue urate deposition, renal calculi, or uric acid nephropathy in patients with leukemias, lymphomas and malignancies who are receiving cancer chemotherapy with its resultant elevating effect on serum uric acid levels.

CONTRAINDICATIONS: Use in children with the exception of those with hyperuricemia secondary to malignancy. The drug should not be employed in nursing mothers.
Patients who have developed a severe reaction to Zyloprim should not be restarted on the drug.
WARNINGS: ZYLOPRIM SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH OR ANY SIGN OF ADVERSE REACTION.
In some instances a skin rash may be followed by more severe hypersensitivity reactions such as exfoliative, urticarial and purpuric lesions as well as Stevens-Johnson syndrome (erythema multiforme) and very rarely a generalized vasculitis which may lead to irreversible hepatotoxicity and death.
A few cases of reversible clinical hepatotoxicity have been noted and in some patients asymptomatic rises in serum alkaline phosphatase or serum transaminase have been observed. Accordingly, periodic liver function tests should be performed during the early stages of therapy, particularly in patients with pre-existing liver disease.
Patients should be alerted to the need for due precautions when engaging in activities where alertness is mandatory.
Occasional cases of hypersensitivity have been reported in patients with renal compromise receiving thiazides and Zyloprim concurrently. For this reason, in this clinical setting, such combination should be administered with caution.
In patients receiving Purinethol® (mercaptopurine) or Imuran® (azathioprine), the concomitant administration of 300-600 mg of Zyloprim per day will require a reduction in dose to approximately one-third to one-fourth of the usual dose of mercaptopurine or azathioprine. Subsequent adjustment of doses of Purinethol or Imuran should be made on the basis of therapeutic response and any toxic effects.
Usage in Pregnancy and Women of Childbearing Age:
Zyloprim should be used in pregnant women or women of childbearing age only if the potential benefits to the patient are weighed against the possible risk to the fetus.
PRECAUTIONS: Some investigators have reported an increase in acute attacks of gout during the early stages of allopurinol administration, even when normal or subnormal serum uric acid levels have been attained.
It has been reported that allopurinol prolongs the half-life of the anticoagulant, dicumarol. This interaction should be kept in mind when allopurinol is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed.
A fluid intake sufficient to yield a daily urinary output of at least 2 liters and the maintenance of a neutral or, preferably, slightly alkaline urine are desirable to (1) avoid the theoretic possibility of formation of xanthine calculi under the influence of Zyloprim therapy and (2) help prevent renal precipitation of urates in patients receiving concomitant uricosuric agents.
Patients with impaired renal function require less drug and should be carefully

"The most important therapeutic measure is the administration of a drug which will block urate synthesis. The agent available at present is allopurinol (Zyloprim...) which is very effective and of low toxicity."[3]

—Alfred Jay Bollet, MD

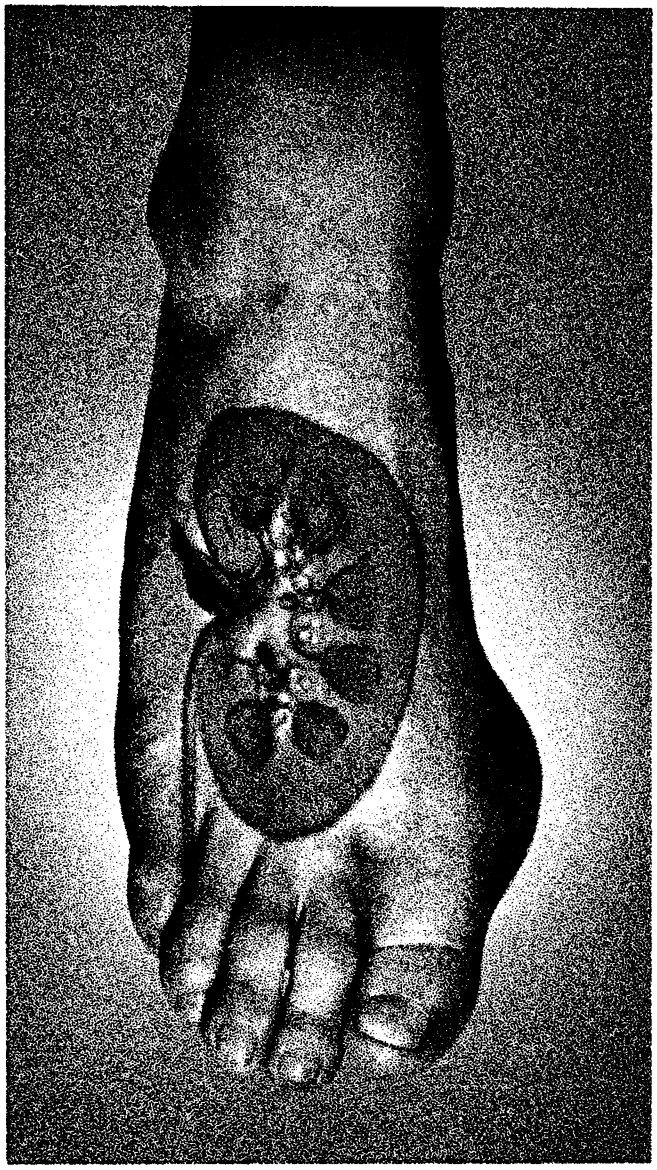
"...allopurinol treatment appears to retard the progression of renal dysfunction."[4]

—T. Gibson, MD et al

LOW INCIDENCE OF TOXICITY

"Clinical experience with allopurinol suggests that most patients tolerate this drug well—a finding strongly supported by our data. Undesired or unintended effects of therapy were reported in only 1.8% of 1835 consecutive recipients."[5]

—G. T. McInnes, MD



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Research Triangle Park
North Carolina 27709

observed during the early stages of Zyloprim administration and the drug withdrawn if increased abnormalities in renal function appear.

In patients with severely impaired renal function, or decreased urate clearance, the half-life or oxipurinol in the plasma is greatly prolonged. Therefore, a dose of 100 mg per day or 300 mg twice a week, or perhaps less, may be sufficient to maintain adequate xanthine oxidase inhibition to reduce serum urate levels. Such patients should be treated with the lowest effective dose, in order to minimize side effects.

Mild reticulocytosis has appeared in some patients.

Periodic determination of liver and kidney function and complete blood counts should be performed especially during the first few months of therapy.

ADVERSE REACTIONS:

Dermatologic: Because in some instances skin rash has been followed by severe hypersensitivity reactions, it is recommended that therapy be discontinued at the first sign of rash or other adverse reaction (see WARNINGS). Skin rash, usually maculopapular, is the adverse reaction most commonly reported. The incidence of skin rash may be increased in the presence of renal disorders.

Exfoliative, urticarial and purpuric lesions, Stevens-Johnson syndrome (erythema multiforme) and toxic epidermal necrolysis have also been reported.

A few cases of alopecia with and without accompanying dermatitis have been reported.

In some patients with a rash, restarting Zyloprim (allopurinol) therapy at lower doses has been accomplished without untoward incident.

Gastrointestinal: Nausea, vomiting, diarrhea, and intermittent abdominal pain have been reported.

Hepatic: Rare cases of granulomatous hepatitis and hepatic necrosis have been reported.

Vascular: There have been rare instances of a generalized hypersensitivity vasculitis or necrotizing angiitis which have led to irreversible hepatotoxicity and death.

Hematopoietic: Agranulocytosis, anemia, aplastic anemia, bone marrow depression, leukopenia, pancytopenia and thrombocytopenia have been reported in patients, most of whom received concomitant drugs with potential for causing these reactions. Zyloprim has been neither implicated nor excluded as a cause of these reactions.

Renal: Rare cases of renal failure have been reported in hypertensive patients who received thiazides and Zyloprim concurrently. Some patients had evidence of hypersensitivity to allopurinol.

Neurologic: There have been a few reports of peripheral neuritis occurring while patients were taking Zyloprim. Drowsiness has also been reported in a few patients.

Ophthalmic: There have been a few reports of cataracts found in patients receiving Zyloprim. It is not known if the cataracts predated the Zyloprim therapy. "Toxic" cataracts were reported in one patient who also received an anti-inflammatory agent; again, the time of onset is unknown. In a group of patients followed by Gutman and Yü for up to five years on Zyloprim therapy, no evidence of ophthalmologic effect attributable to Zyloprim was reported.

Drug Idiosyncrasy: Symptoms suggestive of drug idiosyncrasy have been reported in a few patients. This was characterized by fever, chills, leukopenia or leukocytosis, eosinophilia, arthralgias, skin rash, pruritus, nausea and vomiting.

OVERDOSAGE: Massive overdosing, or acute poisoning, by Zyloprim has not been reported.

HOW SUPPLIED: 100 mg (white) scored tablets, bottles of 100 and 1000; 300 mg (peach) scored tablets, bottles of 30, 100 and 500. Unit dose packs for each strength also available.

Complete information available from your local B. W. Co. Representative or from Professional Services Department PML.

U.S. Patent No. 3,624,205 (Use Patent)

Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

* **WARNING**
This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function.

Thiazides may add to or potentiate the action of other antihypertensive drugs.

Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

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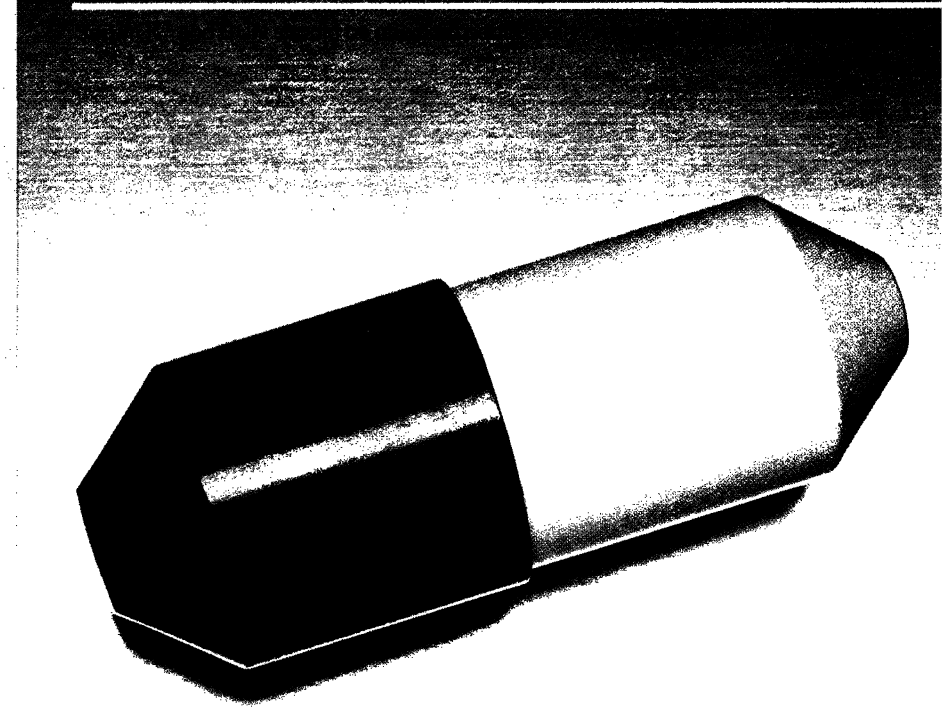

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Each capsule contains 50 mg. of Dyrenium® (brand of triamterene) and 25 mg. of hydrochlorothiazide.

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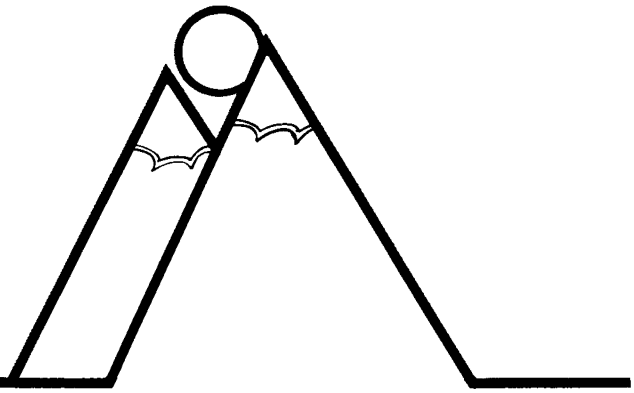

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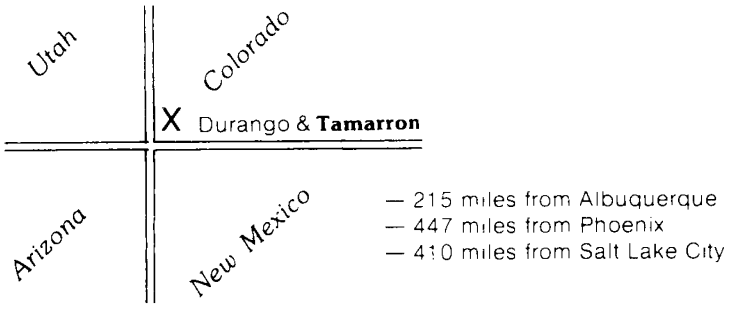

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TI•SCREEN is a unique new PABA - free, non-sensitizing sunscreen developed by dermatologists to meet the demanding needs of sun sensitive skin. A combination of two effective ultraviolet absorbers in a moisturizing base provide the ultimate in sunburn protection. TI•SCREEN is formulated to resist removal by water immersion or perspiration, so that the desired protection will be lasting, yet is easily washed off with soap and water, and leaves no PABA stain.

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Now a choice —

a prescription-only product for the treatment of common warts.

- Available on Rx only
- Effective, safe, simple to use
- Available in ½ fl. oz. (15 ml) dropper bottle

Usage: TiFlex is a prescription-only wart removal product that is very effective in eradicating the common wart.

Description: TiFlex contains a high concentration of salicylic acid 17% and lactic acid 17%, in a flexible collodion suspension. This potent combination makes TiFlex an efficacious keratolic agent for the removal of benign epithelial tumors, such as common warts.

Contraindications: Diabetics or patients with impaired blood circulation should not use TiFlex. Do not use on moles, birthmarks or unusual warts with hair growing from them.

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Additional Prescribing Information on Request.

Preferred by Consumers

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Each prolonged action tablet contains: Phenylephrine Hydrochloride 25 mg • Phenylpropanolamine Hydrochloride 50 mg • Chlorpheniramine Maleate 8 mg • Hyoscyamine Sulfate 0.19 mg • Atropine Sulfate 0.04 mg • Scopolamine Hydrobromide 0.01 mg • Each Ru-Tuss tablet acts continuously for 10 to 12 hours.

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Please see brief summary of prescribing information on the next page.

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Caution patients about driving, operating hazardous machinery or drinking alcohol during therapy. Limit dose to 15 mg in elderly or debilitated patients. Contraindicated during pregnancy.

Dalmane® (IV)

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15-mg/30-mg capsules

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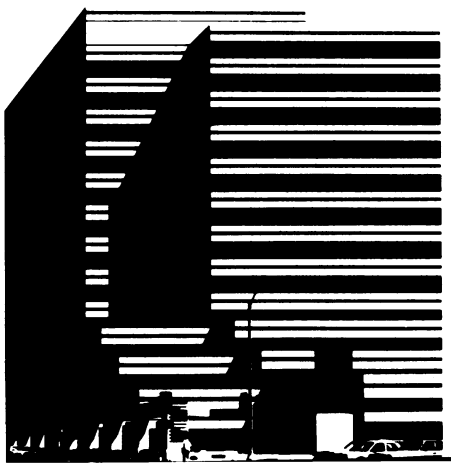

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Salary commensurate with experience, and includes a pension and bonus program. Write with your curriculum vitae to: **Kendall E. Phelps, Administrator of Health Plan and Clinic, P.O. Box 7883, San Francisco, CA 94120. All replies will be kept in confidence.**

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NEUROLOGIST - OBSTETRICIAN/GYNECOLOGIST. To join progressive eighteen physician multispecialty clinic in sunny southeastern New Mexico. Modern facility in friendly, growing community of 40,000. Good salary plus incentive bonus paid on production. Many excellent benefits including insurance, paid vacations and continuing education, stock option offered. Immediate opening, call (505) 392-5571, or send CV to Melba Greer, Recruiting Director, Norte Vista Medical Center, Ltd., 2410 North Fowler, Hobbs, NM 88240.

EMERGENCY MEDICINE: California coastal community hospital in beautiful Humboldt County seeks full-time staff physician for low volume emergency department. Competitive guaranteed income, professional liability insurance, CME tuition and ACEP dues provided. Relocation to this gorgeous recreational area a must. For details contact Ms Billie Warren in confidence at: Spectrum Emergency Care, Inc., 606 Wilshire Blvd., Suite 416, Santa Monica, CA 90401; (213) 451-5481 or 1 (800) 421-6655.

SAN LUIS OBISPO—CARDIOLOGIST position open with 37-member multi-specialty group; include non-invasive and invasive; some satellite office practice. Excellent practice opportunity; full range of benefits; early Shareholder status; all practice costs paid. For more information: contact D. R. Molesworth, Administrator or Steven C. Pontius, MD, 1235 Osos St., San Luis Obispo, CA 93401; (805) 546-5600.

PHYSICIANS WANTED

SAN DIEGO STATE UNIVERSITY STUDENT HEALTH CENTER—Physician II—Family Practitioner. Board eligible or certified Family Physician for comprehensive ambulatory facility serving 30,000 students. 10 month salary—$40,-500-49,000; 12 month salary—$48,500-58,824. Inquiries with CV to Kevin Patrick, MD, MS, Director, Student Health Services, SDSU, San Diego, CA 92182.

PARTNER/ASSOCIATE wanted for growing urgent care center near San Francisco. Excellent opportunity for experienced family practitioner or emergency physician to become established in the Bay Area. Possibility exists for affiliation with a San Francisco Hospital Emergency Department group. Send inquiries and information to C. M. Reese, 1001 Sneath Lane, Suite 104, San Bruno, CA 94066.

WANTED: OTOLARYNGOLOGIST! Want to practice where physicians are still in relatively short supply? Want to work in an area where your services are needed, appreciated and well remunerated? I am a 53-year-old Otolaryngologist with a fabulous practice and heart trouble. I am looking for a partner and successor. This is a very worthwhile opportunity in Middle Georgia for the right person. If the situation seems interesting to you, please write with CV and goals to: Wentford A. Spears, MD, Suite C, 212 Hospital Drive, Warner Robins, GA 31093; (912) 823-0106.

MINOR EMERGENCY CLINICS: Full-time physician openings for Fair Oaks (Sacramento area) and Vacaville (near Napa Valley) clinics. New modern facilities. Malpractice coverage provided. Call Dr Kendall Bauer evenings, (916) 933-1449.

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FAMILY PRACTITIONER, APPLE VALLEY, CA—Large well-established comprehensive family practice seeking board certified family practitioner. Active inpatient practice—hospital next door. Some OB required. Prepaid programs and industrial medicine. Rural community free of smog. Salary percentage of billings with partnership option. Malpractice provided. Minimum two-year commitment.

ANESTHESIOLOGIST—Tremendous opportunity immediately available. Well reputable hospital located in western part of Arizona seeking a Chief Anesthesiologist. Must have current AZ license and DEA certificate.

EMERGENCY PHYSICIANS, HIGH DESERT, CA—New Hospital-sponsored satellite Urgent Care Center seeking two full time family practice-oriented emergency physicians for July, 1983 placement. Located in rapidly growing community. Some followup care required. Twelve hours/day, 7 days/week. Guarantee plus percentage program. Equity available. Malpractice provided. Must have current CA license, DEA certificate and ACLS certificate. Minimum two-year commitment.

For above three specialties call or write: **ROSEMARY RYAN, PACIFIC SERVICES, P.O. BOX 1346, LOMA LINDA, CA 92354; (714) 825-4401.**

(Continued on Page 128)

Immediate Opening
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Excellent Opportunity in the Best of the Southwest!
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Duties: Care for acute illnesses and injuries; minor surgery and wound repair, supervise ancillary personnel; participate in our infirmary and 24-hour emergency care services (for extra compensation). Requirements: complete one year internship and one year experience of increasing responsibility; current valid California license to practice medicine. Closing Date: July 20, 1983.

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ADDRESS (HOME)			HOME PHONE/AREA CODE
CITY	STATE	ZIP CODE	YEARS ☐ RENT ☐ OWN
MORTGAGE HOLDER			YOUR SOCIAL SECURITY NO.
PROFESSION OR EMPLOYMENT			
BUSINESS ADDRESS			BUSINESS PH. / AREA CODE
CITY	STATE	ZIP CODE	NET ANNUAL INCOME

FINANCIAL INFORMATION

*If any assets listed below are jointly owned with others or any other person has an interest in same, state name of co-owner, or co-party of interest, and % of interest by specific asset.

ASSETS		LIABILITIES	
REAL ESTATE (LIST ADDRESSES)	$	REAL ESTATE MORTGAGES (LIST FIRM & ADDRESS)	$
CASH & ACCTS. RECEIVABLE (LIST)		LOANS & ACCTS. PAYABLE (LIST)	
STOCKS AND BONDS (LIST)			
AUTOMOBILES (LIST)		BUSINESS EQUIPMENT & LEASES	
OTHER ASSETS (LIST)		OTHER DEBTS & ANY CONTINGENT LIABILITIES (LIST)	
TOTAL ASSETS	$	**TOTAL LIABILITIES**	$
		NET WORTH	$

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(Not applicable to residents of AR, NC, OR, WA, AK & HI. CA residents $10,000 minimum—personal, family or household loans only.)

WJ7/83

(Continued from Page 126)

PHYSICIANS WANTED

OPHTHALMOLOGY FELLOW . . . Anterior Segment Fellowship in buy private practice associated with Medical College. Intraocular Lens Implantation, Including posterior chamber and anterior chamber lenses. Extracapsular and Phacoemulsification techniques. $40,000 plus fringes. Send CV and career objectives to Box 6342, Western Journal of Medicine, 731 Market St., San Francisco, CA 94103.

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SAN FRANCISCO BAY AREA—Part-time emergency room position for physician with ER training and/or experience. Forty minutes from San Francisco. Larry Casalino Phone (415) 726-4432.

GENERAL INTERNIST, excellent opportunity for a competent, caring, hardworking General Internist to associate with another Board certified Internist. Practice is located in the San Francisco Bay Area and includes an excellent mix of office, hospital and ICU-CCU patients. The mix includes excellent primary care and consulting opportunities. The hospital and office are both well equipped. Please reply Box 6360, Western Journal of Medicine, 731 Market St., San Francisco, CA 94103.

GENERAL SURGEON, GENERAL INTERNIST, Board certified/eligible: Small multi-specialty group, university town central Washington, has space and services available on a lease basis with future partnership anticipated. Contact J. W. Devney, MD, or A. J. Grose, MD, Medical Building Associates, P.O. Box 369, Ellensburg, WA 98926.

PHYSICIANS WANTED

PHYSICIAN WANTED. Internist or FP Physician with interest in cardiology, for small North Idaho clinic. Excellent recreational area. Write to Box 6359, Western Journal of Medicine, 731 Market St., San Francisco, CA 94103.

INTERNIST/RAD/ORTHO SUR/PED/FP/GP for established growing, multi-specialty practice in sunny Los Angeles. Guaranteed salary and benefits first year, then incentive based on productivity. Ownership potential, growth capability. Respond w/CV: C. Kaner, Box 6367, Western Journal of Medicine, 731 Market St., San Francisco, CA 94103.

OB/GYN—TULARE, CALIFORNIA—Board certified eligible OB/GYN to practice in an outpatient clinic with 9 physicians. Consider a rural lifestyle with cultural amenities of metropolitan areas easily accessed and the Sierra Nevada Mountains nearby. Salary: $82,867-$87,090 annually. Send CV to: Tulare County Personnel, Courthouse, Room 106, Visalia, CA 93291; (209) 733-6266. Affirmative Action Employer.

WASHINGTON STATE: Seek third team member to join new ER staff at modern, well-equipped emergency department in Aberdeen. Only 20 miles from Pacific Ocean; 2 hours from Seattle. Outstanding recreation nearby. Excellent guaranteed income, professional liability insurance, CME tuition and ACEP dues reimbursement. ER experience required. Future staff positions will also be available in other northwest locations. For details contact Ms. Billie Warren, Spectrum Emergency Care, Inc., 606 Wilshire Blvd., Suite 416, Santa Monica, CA 90401; in Calif call (213) 451-5481, outside Calif 1 (800) 421-6655.

HEMATOLOGIST-ONCOLOGIST with Boards in both specialties needed in San Francisco Bay Area. Excellent practice situation with ready access to radiation therapy, oncology unit, and NCOG protocols. Send CV and references to Box 6353, Western Journal of Medicine, 731 Market St., San Francisco, CA 94103.

OTOLARYNGOLOGIST—to join prepaid healthplan; multi-specialty group with 370 full-time physicians, 30 healthcare facilities in Los Angeles and Orange Counties. Excellent benefits and salary with 4½ day work week. Professional Placement, INA and Ross Loos Healthplans, 700 N. Brand Blvd., Suite 500-W, Glendale, CA 91203.

MINOR EMERGENCY CLINICS. Full-time physician openings for Fair Oaks (Sacramento area) and Vacaville (near Napa Valley) clinics. New modern facilities. Part-time, fill-in positions also available. Call Dr Kendall Bauer, (916) 933-1449 evenings or write 815 Mast Ct, Folsom, CA 95630.

FAMILY PRACTICE PHYSICIAN for non profit, primary care, community clinic. Pediatric, family, geriatric and gynecology. Half time position to add to our current medical staff. Rewarding work in beautiful Santa Barbara. Additional employment opportunities in the community. Contact: Jenny Koebel, MA, or Andy Gersoff, MD, 628 W. Micheltorena, Santa Barbara, CA 93101; (805) 962-0145.

PHYSICIAN WANTED

GENERAL SURGEON, Board certified or eligible, to join 15 doctor multi-specialty clinic in New Ulm, Minn., historic city of 15,000, located 90 minutes from Minneapolis metro area and 30 minutes from Mankato State University. Agricultural businesses supplemented by 3M Co., Kraft Foods, AMPI, provides stability. Contact Harold Fenske, Adm., collect (507) 354-4101.

PHYSICIAN FOR FOOTHILL COMMUNITY. Good hospital. Fast growing area. Above the smog. Terms. Thurmond & Thurmond, (916) 885-1911 Don Grier.

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BEAUTIFUL NORTHERN SAN DIEGO COUNTY offers unique family practice opportunity. Ambulatory primary care, no call, malpractice, minimum guarantee, fee for service, partnership opportunity. Send résumé to: Box 6365, Western Journal of Medicine, 731 Market St., San Francisco, CA 94103.

BEAUTIFUL SAN FRANCISCO BAY AREA community offers unique family practice opportunity in San Leandro. Ambulatory primary care, no call, malpractice, minimum guarantee, fee for service, partnership opportunity. Send résumé to: Box 6366, Western Journal of Medicine, 731 Market St., San Francisco, CA 94103.

WORLD FAMOUS MAMMOTH MOUNTAIN forms the backdrop for a fabulous opportunity in Family Practice. One half of an active, well-established practice available now. Contact Paul W. Hildebrand, MD, P.O. Box 9, Mammoth Lakes, CA 93546.

CALIFORNIA AND WESTERN STATES. HIGH INCOME practices for sale: Family, OBG, Orthopedic, Internal, Psychiatry, Pediatric, Surgery, Ophthalmology, others. Mary Bradshaw, Prof. Pract. Opportunities, 21 Altamount Dr., Orinda, CA 94563; (415) 376-0762. Sales, Appraisals, Consulting, Placement, Résumé preparation service.

INTERNIST NEEDED: Flagstaff, Arizona. Assume busy Internal Medicine practice, lovely Alpine community of 40,000. Call for details, Tom Davee, MD, (602) 774-2767.

(Continued on Page 130)

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Concept approved by **LACMA.**
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Other *staff leasing companies* **Do Not Compare...**

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V **No officer or stockholder** of PSC is a participant in the employee pension plan.
VI **Lower required deposit.**
VII **No** set-up fees. **No** new employee fees.
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IX Lower actual **net cost** to *staff lease.*

Respectfully Submitted
Eric Jay Selter, Esq.
16000 Ventura Boulevard, Suite 1205
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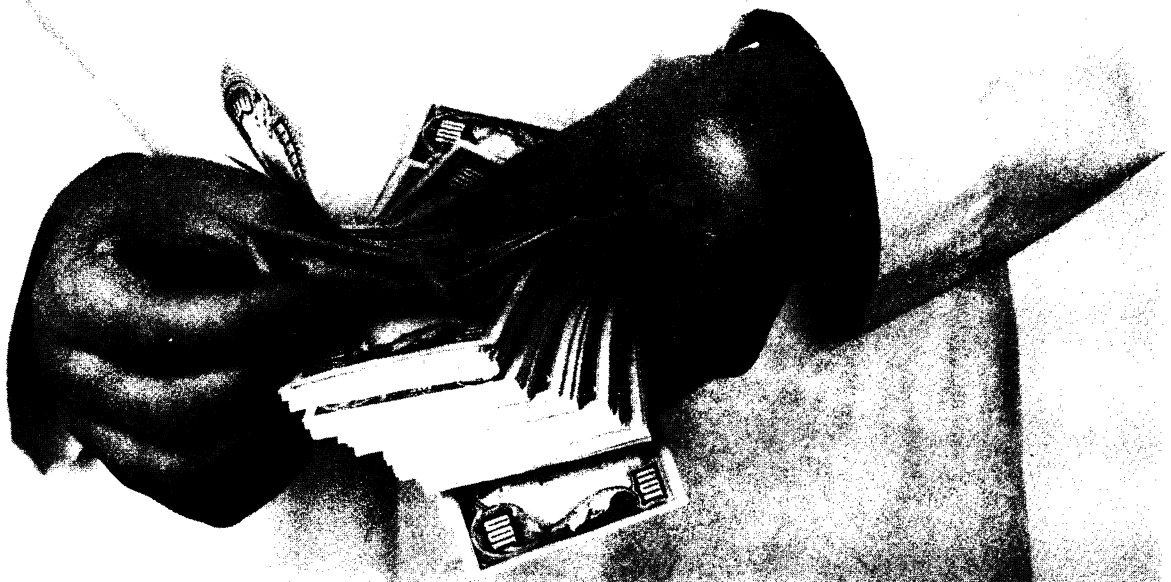

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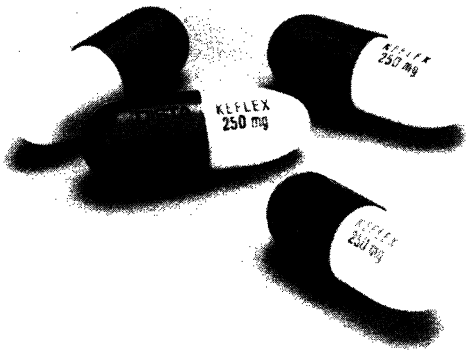
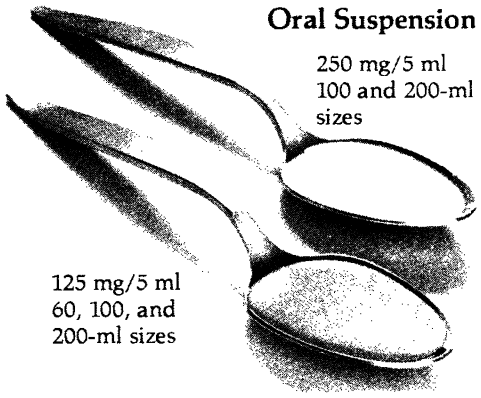


250-mg Pulvules®

Oral Suspension

250 mg/5 ml
100 and 200-ml
sizes



125 mg/5 ml
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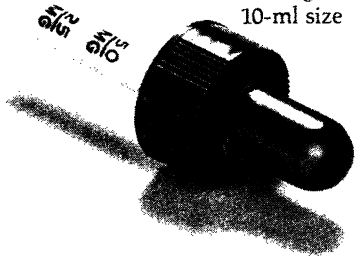

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THE SPASM/PAIN/SPASM CYCLE

In skeletal muscle spasm due to local pathology, responsive to the distinct actions of

Adjunctive VALIUM® (IV) diazepam/Roche

2-mg, 5-mg, 10-mg scored tablets

Advantages cyclobenzaprine cannot claim

—Wider range of indications as adjunctive therapy for skeletal muscle spasm—from spasm due to local pathology (*e.g.*, herniated lumbosacral discs or acute muscle strain) to spasm associated with upper motor neuron disorders (*e.g.*, cerebral palsy, athetosis, stiff-man syndrome).

—May be used adjunctively for relieving skeletal muscle spasm in patients with hyperthyroidism, cardiac patients and patients being treated with anticholinergics or guanethidine-type antihypertensives.

—Can be administered to patients less than 15 years and more than 6 months of age.

—Scored tablets in three strengths provide greater dosage flexibility.

Since drowsiness, fatigue and ataxia sometimes occur, patients should be cautioned against driving or operating hazardous machinery and should also be advised against simultaneous ingestion of alcohol.

References: 1. Rankin EA: *Comm Educ* 3(1):46-50, Jan 1975. **2.** When muscle spasm notches your patient: *Patient Care* 8(11):20-37, Jun 1, 1974.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Management of anxiety disorders, or short-term relief of symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. Symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).
The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.
The clearance of Valium (diazepam/Roche) and certain other benzodiazepines can be delayed in association with Tagamet (cimetidine) administration. The clinical significance of this is unclear.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults:* Anxiety disorders, symptoms of anxiety, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

How Supplied: For oral administration, Valium (diazepam/Roche) scored tablets—2 mg, white; 5 mg, yellow; 10 mg, blue—bottles of 100* and 500;* Prescription Paks of 50, available in trays of 10.* Tel-E-Dose* packages of 100, available in trays of 4 reverse-numbered boxes of 25,* and in boxes containing 10 strips of 10.*

*Supplied by Roche Products Inc., Manati, Puerto Rico 00701
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ROCHE®

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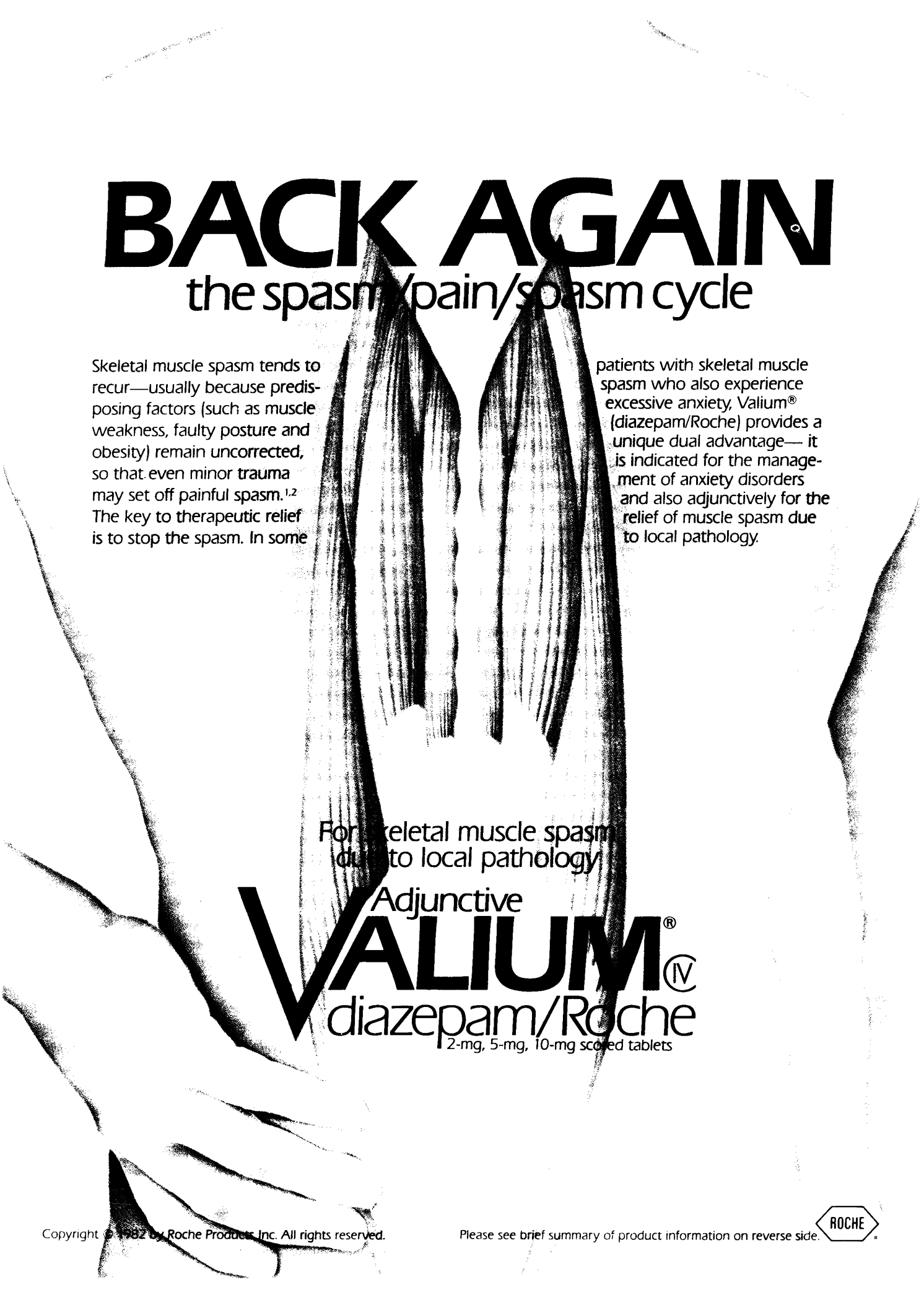
Manati, Puerto Rico 00701

BACK AGAIN

the spasm/pain/spasm cycle

Skeletal muscle spasm tends to recur—usually because predisposing factors (such as muscle weakness, faulty posture and obesity) remain uncorrected, so that even minor trauma may set off painful spasm.[1,2] The key to therapeutic relief is to stop the spasm. In some patients with skeletal muscle spasm who also experience excessive anxiety, Valium® (diazepam/Roche) provides a unique dual advantage— it is indicated for the management of anxiety disorders and also adjunctively for the relief of muscle spasm due to local pathology.



For skeletal muscle spasm due to local pathology

Adjunctive

VALIUM®

(IV)

diazepam/Roche

2-mg, 5-mg, 10-mg scored tablets

Please see brief summary of product information on reverse side.

ROCHE®